### INTERNATIONAL SEARCH REPORT

International application No. PCT/US00/21769

A. CL45	SIFICATION OF SUBJECT MATTER		
	C12Q 1/68; C07H 21/02, 21/04		
	435/6; 536/23.1, 23.5 o International Patent Classification (IPC) or to bot	h national classification and IPC	}
	DS SEARCHED		
	ocumentation searched (classification system followe	ed by classification symbols)	
	435/6; 536/23.1, 23.5		•
Documenta searched	tion searched other than minimum documentation to	the extent that such documents are i	ncluded in the fields
USPT, D	ata base consulted during the international search (no WPI, MEDLINE, CAPLUS, LIFESCI, SCISEARCI ms: interleukin 10, IL10, promoter, allele, polymo	H, BIOSIS, EMBASE	
C. DOC	UMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where a	ppropriate, of the relevant passages	Relevant to claim No.
X	AHERN, H. Biochemical, reagent kit on investment. The Scientist. 24 July especially p. 3/5-4/5.	••	9
X Y A	ESKDALE et al. Mapping of the hu characterization of the 5' flanking s August 1997, Vol. 46, No. 2, pages 1204.	equence. Immunogenetics.	1, 10  9  2-8, 11
X  Y 	MOK et al. Interleukin-10 promoter Chinese patients with systematic lupus Rheumatism. June 1998, Vol. 41, especially Table 3.		3, 7-8  9  1-2, 4-6, 10-11
X Furti	ner documents are listed in the continuation of Box	C. See patent family annex.	
• Sp.	cial categories of cited documents: document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the priority date and not in conflict wit understand the principle or theory w	h the application but cited to
"E"	earlier document published on or after the international filing date	"X" document of particular relevance; the considered novel or cannot be cons step when the document is taken alo	idered to involve an inventive
cit	ument which may throw doubts on priority claim(s) or which is do establish the publication date of another citation or other cital reason (as specified)  document referring to an oral disclosure, use, exhibition	"Y" document of particular relevance: th considered to involve an inventive combined with one or more other such being obvious to a person skilled in	step when the document is A documents, such combination
	or other means	"&" document member of the same pater	
Date of the	ument published prior to the international filing date but later in the priority date claimed actual completion of the international search	Date of mailing of the international s 24 OCT 2000	
Name and Commission	nailing address of the ISA/US ner of Patents and Trademarks	Authorized officer	Callin
Box PCT	1. D.C. 20231	DIANA BLIGHANNSEN	70
Facsimile N		Telephone No. (703) 308-0196	()

### INTERNATIONAL SEARCH REPORT

International application No. PCT/US00/21769

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X  Y 	ROOD et al. Neuropsychiatric systematic lupus erythematosus is associated with imbalance in interleukin 10 promoter haplotypes. Ann. Rheum. Dis. February 1999, Vo. 58, No. 2, pages 85-89, especially p. 87-88.	3, 7-8  9  1-2, 4-6, 10-11
A	COAKLEY et al. Interleukin-10 promoter polymorphisms in rheumatoid arthritis and Felty's syndrome. Brit. J. Rheum. September 1998, Vol. 37, No. 9, pages 988-991.	1-11
A	MYTILINEOS et al. A PCR-SSP method for the detection of polymorphisms in the promoter regions of IL10, TNFA, and TGFB genes. Human Immunol. April 1999, Vol. 60, No. SUPPL 1, page S104.	1-11
A	KEIJSERS et al. IL10 polymorphisms in relation to production and rheumatoid arthritis. Arthritis & Rheumatism. September 1997, Vol. 40, No. 9 SUPPL, page S179.	1-11
A	TOUNTAS et al. Ethnic association of 3 polymorphisms in the IL-10 promoter and inflammatory bowel disease (IBD). Gastroenterology. April 1999, Vol. 116, No. 4, Part 2, page G3617.	1-11



### **PCT**

#### **NOTIFICATION OF ELECTION**

(PCT Rule 61.2)

### From the INTERNATIONAL BUREAU

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlingon, VA 22202

Date of mailing (day/month/year) 10 July 2001 (10.07.01)	ETATS-UNIS D'AMERIQUE in its capacity as elected Office	
International application No. PCT/US00/21769	Applicant's or agent's file reference UAB-16852/22	
International filing date (day/month/year) 09 August 2000 (09.08.00)	Priority date (day/month/year) 09 August 1999 (09.08.99)	
Applicant	-	
KIMBERLY, Robert, P. et al		

1.	The designated Office is hereby notified of its election made:
	X in the demand filed with the International Preliminary Examining Authority on:
	05 March 2001 (05.03.01)
	in a notice effecting later election filed with the International Bureau on:
2.	The election X was
	was not
	made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

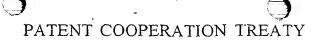
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland

Authorized officer

H. Zhou

Telephone No.: (41-22) 338.83.38

Facsimile No.: (41-22) 740.14.35



From the INTERNATIONAL SEARCHING AUTHORITY

To: ELLEN S. COGEN GIFFORD, KRASS, GROH, SPRINKLE, ANDERSON

# **PCT**

& CITKOWSKI, P.C. 280 N. OLD WOODWARD AVE., STE 400 BIRMINGHAM, MI 48009 US	NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION (PCT Rule 44.1)
	Date of Mailing (day/month/year) <b>24</b> OCT 2000
Applicant's or agent's file reference UAB-16852/22	FOR FURTHER ACTION See paragraphs 1 and 4 below
International application No. PCT/US00/21769	International filing date (day/month/year) 09 AUGUST 2000
Applicant  UAB RESEARCH FOUNDATION	Response out 11-24-00 due 12-24-00
Filing of amendments and statement under Artic	al search report has been established and is transmitted herewith.  le 19: the claims of the international application (see Rule 46):

The applicant is however position that the interesting	Leaguely govern has been parablished and is transmissed by small to
	I search report has been established and is transmitted herewith.
Filing of amendments and statement under Articl The applicant is entitled, if he so wishes, to amend t	the claims of the international application (see Rule 46):
	ents is normally 2 months from the date of transmittal of the more details, see the notes on the accompanying sheet.
Where? Directly to the International Bureau of W 34, chemin des Colombe 1211 Geneva 20, Switzer Facsimile No.: (41-22) 7	ttes Cland
For more detailed instructions, see the notes on	the accompanying sheet.
•	
2. The applicant is hereby notified that no international Article 17(2)(a) to that effect is transmitted herewith	search report will be established and that the declaration under.
3. With regard to the protest against payment of (an)	additional fee(s) under Rule 40.2, the applicant is notified that:
	has been transmitted to the International Bureau together with the has the protest and the decision thereon to the designated Offices.
no decision has been made yet on the protest;	the applicant will be notified as soon as a decision is made.
4. Further action(s): The applicant is reminded of the fol	llowing:
If the applicant wishes to avoid or postpone publication	ational application will be published by the International Bureau. a, a notice of withdrawal of the international application, or of the provided in rules 90 bis 1 and 90 bis 3, respectively, before the nal publication.
Within 19 months from the priority date, a demand for in wishes to postpone the entry into the national phase un	ternational preliminary examination must be filed if the applicant till 30 months from the priority date (in some Offices even later).
	oust perform the prescribed acts for entry into the national phase ted in the demand or in a later election within 19 months from the not bound by Chapter II.
Name and mailing address of the ISA/US	Authorized office All Com
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	DIANA B. JOHANNSEN
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0125

Form PCT/ISA/220 (July 1998)★

GIFFORD, KRASS, GROH, SPRINKLE,



## PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To: ELLEN S. COGEN GIFFORD, KRASS, GROH, SPRINKLE, ANDERSON & CITKOWSKI, P.C. 280 N. OLD WOODWARD AVE., STE 400 BIRMINGHAM, MI 48009 US	PCT  NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION  (PCT Rule 44.1)		
	(day/month/year) 24 OCT 2000		
Applicant's or agent's file reference  UAB-16852/22	FOR FURTHER ACTION See paragraphs 1 and 4 below		
	International filing date		
International application No.	(day/month/year)		
PCT/US00/21769	09 AUGUST 2000		
Applicant  UAB RESEARCH FOUNDATION			
Filing of amendments and statement under Article	search report has been established and is transmitted herewith. e 19: the claims of the international application (see Rule 46):		
When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report; however, for more details, see the notes on the accompanying sheet.			
Where? Directly to the International Eureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35			
For more detailed instructions, see the notes on			
2. The applicant is hereby notified that no international Article 17(2)(a) to that effect is transmitted herewith.	search report will be established and that the declaration under		
3. With regard to the protest against payment of (an)	additional fee(s) under Rule 40.2, the applicant is notified that:		
applicant's request to forward the texts of both	as been transmitted to the International Bureau together with the the protest and the decision thereon to the designated Offices.		
no decision has been made yet on the protest;	the applicant will be notified as soon as a decision is made.		
4. Further action(s): The applicant is reminded of the following:			
If the applicant wishes to avoid or postpone publication	ational application will be published by the International Bureau., a notice of withdrawal of the international application, or of the provided in rules 90 bis 1 and 90 bis 3, respectively, before the hall publication.		
Within 19 months from the priority date, a demand for in wishes to postpone the entry into the national phase un	ternational preliminary examination must be filed if the applicant til 30 months from the priority date (in some Offices even later).		
Within 20 months from the priority date, the applicant m before all designated Offices which have not been elect priority date or could not be elected because they are	ust perform the prescribed acts for entry into the national phase ed in the demand or in a later election within 19 months from the not bound by Chapter II.		
Name and mailing address of the ISA/US	Authorized office;		
Commissioner of Patents and Trademarks Box PCT	DIANAB. JOHANNSEN		
Washington, D.C. 20231 Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196		

Form PCT/ISA/220 (July 1998)\*

(See notes on accompanying sheet)

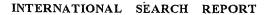


## **PCT**

### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference UAB-16852/22	FOR FURTHER ACTION	see Notification of (Form PCT/ISA/22	Transmittal of International Search Report 0) as well as, where applicable, item 5 below.
International application No.	International filing da	te (day/month/year)	(Earliest) Priority Date (day/month/year)
PCT/US00/21769	09 AUGUST 2000	•	09 AUGUST 1999
Applicant UAB RESEARCH FOUNDATION			
This international search report has bee according to Article 18. A copy is being the This international search report consists.  X It is also accompanied by a search report.	and transmitted to the Interest of a total of $\frac{4}{3}$ shee	rnational Bureau.	uthority and is transmitted to the applicant report.
1. Basis of the report			
a. With regard to the language, t language in which it was filed	, unless otherwise indicate	d under this item.	asis of the international application in the
b. With regard to any nucleotide was carried out on the basis o		nce disclosed in the i	nternational application, the international search
contained in the internation	al application in written t	orm.	
filed together with the inter	national application in co	mputer readable for	n.
furnished subsequently to the	nis Authority in written f	orm.	•
furnished subsequently to the	his Authority in computer	readable form.	
international application as	filed has been furnished.		s not go beyond the disclosure in the
2. Certain claims were found	l unsearchable (See Bo)	( I).	
3. Unity of invention is lack	ing (See Box II).		
4. With regard to the title,			
x the text is approved as sub-	mitted by the applicant.		
the text has been establishe	d by this Authority to rea	ad as follows:	
5. With regard to the abstract,			
the text is approved as sub-	mitted by the applicant.		
the text has been established Box III. The applicant may search report, submit common search report.	d, according to Rule 38.2 within one month from t		
6. The figure of the drawings to be p	oublished with the abstrac	t is Figure No. 3	
X as suggested by the applica			None of the figures.
because the applicant failed	l to suggest a figure.		
because this figure better c	haracterizes the invention	l.	





International application No. PCT/US00/21769

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

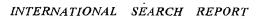
### **NEW ABSTRACT**

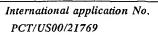
A process and a package for identifying single nucleotide polymorphisms in interleukin-10 (IL-10) are useful in identifying individual susceptibility to a disease. IL-10 is active in the immune response and autoimmune diseases. The susceptibility and severability of autoimmune disease is determined by genotyping or phenotyping an individual IL-10 promoter region. Figure 3 is a graph showing association of -3575A/-2763A SNP haplotype with production of IL-10 by donors, segregated by distal SNP haplotypes.

### INTERNATIONAL SEARCH REPORT

International application No. PCT/US00/21769

A. CLASSIFICATION OF SUBJECT MATTER  IPC(7) :C12Q 1/68; C07H 21/02, 21/04  US CL :435/6; 536/23.1, 23.5	•	
US CL: 435/6; 536/23.1, 23.5 According to International Patent Classification (IPC) or to	both national classification and IPC	
B. FIELDS SEARCHED		
Minimum documentation searched (classification system foll	lowed by classification symbols)	
U.S. : 435/6; 536/23.1, 23.5		
Documentation searched other than minimum documentation	n to the extent that such documents are	ncluded in the fields
searched		······································
Electronic data base consulted during the international search	(name of data base and, where practicabl	e, search terms used)
USPT, DWPI, MEDLINE, CAPLUS, LIFESCI, SCISEAL search terms: interleukin 10, IL10, promoter, allele, poly		75, -2849, -2763
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category* Citation of document, with indication, when	re appropriate, of the relevant passages	Relevant to claim No.
X AHERN, H. Biochemical, reagent on investment. The Scientist. 24 July especially p. 3/5-4/5.	•	9
characterization of the 5' flanking	ESKDALE et al. Mapping of the human IL10 gene and further characterization of the 5' flanking sequence. Immunogenetics. August 1997, Vol. 46, No. 2, pages 120-128, especially Fig. 1, Fig. 4.	
X MOK et al. Interleukin-10 promote Chinese patients with systematic lup Rheumatism. June 1998, Vol. 4 especially Table 3.		3, 7-8  9  1-2, 4-6, 10-11
X Further documents are listed in the continuation of E	Sox C. See patent family annex.	
Special categories of cited documents:	"T" later document published after the	international filing date or
"A" document defining the general state of the art which not considered to be of particular relevance	priority date and not in conflict wi is understand the principle or theory u	th the application but cited to nderlying the invention
"E" earlier document published on or after the international filing date	step when the document is taken alo	idered to involve an inventive
"L" document which may throw doubts on priority claim(s) or which cited to establish the publication date of another citation or othe special reason (as specified)	er "Y" document of particular relevance; the considered to involve an inventive combined with one or more other suc	step when the document is hocuments, such combination
"O" document referring to an oral disclosure, use, exhibitio or other means		
"P" document published prior to the international filing date but late		
Date of the actual completion of the international search  26 SEPTEMBER 2000	Date of mailing of the international s  24 OCT 2000	earch report
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT	Authorized officer DIANA BUOHANNSEN	Collingo
Washington, D.C. 20231 Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196	X
Facsimile No. (703) 305-3230	100phono 110. (700) 500-0150	1 /





Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
	of wormon, wine marcaison, where appropriate, of the recevant passages	Acterum to claim 140
K 	ROOD et al. Neuropsychiatric systematic lupus erythematosus is associated with imbalance in interleukin 10 promoter haplotypes.	3, 7-8
 t	Ann. Rheum. Dis. February 1999, Vo. 58, No. 2, pages 85-89, especially p. 87-88.	9    1-2, 4-6, 10-11
	COAKLEY et al. Interleukin-10 promoter polymorphisms in rheumatoid arthritis and Felty's syndrome. Brit. J. Rheum. September 1998, Vol. 37, No. 9, pages 988-991.	1-11
	MYTILINEOS et al. A PCR-SSP method for the detection of polymorphisms in the promoter regions of IL10, TNrA, and TGFB genes. Human Immunol. April 1999, Vol. 60, No. SUPPL 1, page S104.	1-11
	KEIJSERS et al. IL10 polymorphisms in relation to production and rheumatoid arthritis. Arthritis & Rheumatism. September 1997, Vol. 40, No. 9 SUPPL, page S179.	1-11
	TOUNTAS et al. Ethnic association of 3 polymorphisms in the IL-10 promoter and inflammatory bowel disease (IBD). Gastroenterology. April 1999, Vol. 116, No. 4, Part 2, page G3617.	1-11 .
}		